## Remarks and Arguments

Amendments to the Claims

Claim 16 has been amended to recite a method for treating a localized bacterial infection, a bacterial-related disease, or both. Support for this amendment is found throughout the specification, for example in paragraph [0023] of the published application.

Claim 16 has also been amended to recite locally administering a therapeutically effective amount of a composition comprising at least one GM-CSF polypeptide. Support for this amendment is found throughout the specification, for example in paragraph [0029] of the published application.

Claim 29 has been amended to recite a composition for locally treating a localized bacterial infection, a bacterial related disease, or both. Support for this amendment is found throughout the specification, for example in paragraphs [0023] and [0029] of the published application.

Amendments to claims 22 and 27 have been made to improve syntax.

New claims 30 and 31 have been added. Support for these claims is found in previously pending claims 16 and 29, respectively.

No new matter has been added as a result of the present amendments to the claims.

Objections to the Claims

The Examiner has objected to claims 16, 22 and 27, and has suggested deleting the word "the" before "GM-CSF." Claims 16, 22 and 27 have been amended per the Examiner's suggestion.

The Examiner also asserts that since more than one GM-CSF polypeptide is present in the art, reciting a sequence identifier along with the claim term "GM-CSF" is necessary. Applicant submits that one of ordinary skill in the art would understand what is meant by the claim term "GM-CSF" without the need for a sequence identifier. For example, paragraph [0024] of the specification describes several types of well known colony stimulating factors (CSFs) including Granulocyte-Colony Stimulating Factor (G-CSF), Macrophage-Colony Stimulating Factor (M-CSF), Granulocyte-Macrophage-Colony Stimulating Factor (GM-CSF) or a multi-Colony

Stimulating Factor (multi-CSF). In paragraph [0036], the specification describes the different biological properties of the various CSFs, including GM-CSF. One of ordinary skill in the art would thus be able to identify the various CSFs and to differentiate GM-CSF from the others.

In paragraph [0037], various methods of making recombinant GM-CSFs are described, and exemplary references disclosing GM-CSF are disclosed. Moreover, in paragraph [0038] commercially available GM-CSFs are described. Thus, one of ordinary skill in the art, in reading the specification in combination with the known state of the art, would be able to easily identify GM-CSFs. As an example of the ease with which one of ordinary skill in the art would be able to identify a GM-CSF, Applicant submits with this response for the Examiner's consideration a supplemental IDS citing an NCBI report describing GM-CSF.

Thus, one of ordinary skill in the art would be aware, both from general knowledge in the art and from the present application, of what a GM-CSF is, would be able to identify it as such, and would therefore understand what is meant by the claim term "GM-CSF." As such, Applicant submits that a specific sequence identifier associated with GM-CSF is not necessary.

Rejections under 35 U.S.C. §112, First Paragraph

*Written Description*

Claims 16-18, 21-27, and 29 have been rejected under 35 U.S.C. §112, first paragraph for failing to comply with the written description requirement. Specifically, the Examiner asserts that the application only sets forth a GM-CSF, and therefore does not provide adequate support for "any GM-CSF fragment, or a derivative of GM-CSF". Without conceding the merits of the rejection, independent claims 16 and 29 have been amended to delete recitation of GM-CSF fragments. This amendment is made without prejudice and Applicant reserves the right to pursue any subject matter canceled as a result of this amendment in future prosecution, either in this application or in one or more continuing applications.

New claims 30 and 31 have been added, reciting a method and composition, respectively, comprising a derivative of a granulocyte-macrophage-colony stimulating factor (GM-CSF) polypeptide. Applicant submits that derivatives of GM-CSF were well known to those of ordinary skill in the art at the time the present application was filed. As but one example, Applicant submits with this response a supplemental IDS containing a reference by Knusli *et al.*

*(Polyethylene glycol (PEG) modification of granulocyte-macrophage colony stimulating factor (GM-CSF) enhances neutrophil priming activity but not colony stimulating activity*, British Journal of Haematology, 82: 654-663, 1992) showing that a PEG-modified derivative of GM-CSF has biological activity that in certain respects is even better than the biological activity of non-PEG-modified GM-CSF.

Paragraph [0039] discloses that "any CSFs analogs or derivatives endowed with comparable or enhanced in vivo biological activity can be used in accordance with the present invention. CSF analogs may be generated by the deletion, insertion, or substitution of amino acids in the primary structure of the naturally occurring glycoproteins, or by chemical modification of the glycoprotein." (emphasis added). As indicated above, Knusli *et al.* describe exemplary PEG-modified derivatives of GM-CSF.

Applicant thus submits that derivatives of GM-CSF were well known in the art at the time the present application was filed. As such, in light of the various derivatives of GM-CSF described in the present application, including chemically modified derivatives, as well as the state of the art exemplified by Knusli *et al.*, one of ordinary skill in the art would be aware that Applicant was in possession of the GM-CSF derivatives recited in claims 30 and 31.

Applicant thus asserts that the presently pending claims comply with the written description requirement of 35 U.S.C. §112, first paragraph and respectfully requests withdrawal of the present rejection.

*Enablement*

Claims 16-18, 21-27, and 29 have been rejected under 35 U.S.C. §112, first paragraph for failing to comply with the enablement requirement. Specifically, the Examiner asserts that the specification, while being enabling for a method of treating a mammal suffering from gingivitis comprising administering a therapeutically effective amount of GM-CSF, does not enable treating any bacterial-related disease by administering a composition comprising GM-CSF, a fragment or derivative thereof.

Without conceding the merits of the rejection, independent claims 16 and 29 have been amended to delete recitation of GM-CSF fragments. This amendment is made without prejudice and Applicant reserves the right to pursue any subject matter canceled as a result of this

amendment in future prosecution, either in this application or in one or more continuing applications.

New claims 30 and 31 have been added, reciting a method and composition, respectively, comprising a derivative of a granulocyte-macrophage-colony stimulating factor (GM-CSF) polypeptide. As described above and as exemplified by Knusli *et al.*, GM-CSF derivatives were known in the art at the time the present application was filed. Taking the disclosure of paragraph [0039] in light of the state of the art exemplified by Knusli *et al.*, one of ordinary skill in the art would be able to practice the presently claimed methods without undue experimentation.

The Examiner further asserts that "the specification does not teach that compositions comprising GM-CSF when administered locally at the site of infection (e.g., orally for treating a periodontal disease) can treat a bacterial-related disease anywhere in the body, in particular, if the composition is not accessible to said site of infection." Applicant traverses this rejection.

Applicant first notes that independent claim 16 has been amended to recite a method for treating a localized bacterial infection, a bacterial-related disease, or both comprising locally administering a composition comprising a therapeutically effective amount of a GM-CSF polypeptide, while independent claim 29 has been amended to recite a composition comprising a therapeutically effective amount of a GM-CSF polypeptide for locally treating a localized bacterial infection, a bacterial related disease, or both.

Applicant submits that the currently pending claims are enabled by the specification, particularly when taken in light of the level of ordinary skill in the art. One of ordinary skill in the art would certainly be aware of which sites in the body are amenable to local administration of a GM-CSF polypeptide for treating a localized bacterial infection, a bacterial related disease, or both, and would be able to employ suitable techniques and reagents to effect such localized administration. Indeed, the specification successfully exemplifies two diverse bacterial diseases, periodontal disease and chronic sinusitis (see Examples 1 and 2), that can be treated using the presently claimed methods and compositions.

Paragraph [0034] of the specification provides further guidance regarding localized bacterial infection and bacterially related disease:

Consequently, the present invention relates to a medicament and a method for the treatment of a localized bacterial infection and bacterial related disease. The expression "Localized bacterial infection and bacterial related disease", as used herein refers to a bacterial infection and bacterial related disease that essentially afflict a limited area of the body of a mammal. Thus, whereas periodontal diseases and sinusitis are localized bacterial infections and bacterial related diseases, e.g. septicaemia is not.

No undue experimentation would be required to identify sites in the body are amenable to local administration of a GM-CSF polypeptide. Moreover, no undue experimentation would be required to actually administer a GM-CSF polypeptide to such sites to treat a localized bacterial infection, a bacterial related disease, or both, as recited in the currently pending claims.

Applicant thus asserts that the presently pending claims comply with the enablement requirement of 35 U.S.C. §112, first paragraph and respectfully requests withdrawal of the present rejection.

Rejections under 35 U.S.C. §102

Claims 16, 21-27, and 29 have been rejected under 35 U.S.C. §102 as being anticipated by Grabstein *et al.* (US Patent No. 5,162,111). Applicant traverses this rejection.

Independent claim 16 has been amended to recite a method for treating a localized bacterial infection, a bacterial-related disease, or both comprising locally administering a composition comprising a therapeutically effective amount of a GM-CSF polypeptide, while independent claim 29 has been amended to recite a composition comprising a therapeutically effective amount of a GM-CSF polypeptide for locally treating a localized bacterial infection, a bacterial related disease, or both.

In contrast, Grabstein *et al.* disclose only systemic administration of GM-CSF, e.g. to treat mice infected with lethal doses of *S. typhimurium* (see Examples 1-4). Grabstein *et al.* fail to teach or suggest methods for treating a localized bacterial infection, a bacterial-related disease, or both comprising locally administering a composition comprising a therapeutically effective amount of a GM-CSF polypeptide, or compositions comprising a therapeutically effective

amount of a GM-CSF polypeptide for locally treating a localized bacterial infection, a bacterial related disease, or both, as recited by the currently pending claims.

As such, Grabstein *et al.* do not anticipate or render obvious the currently pending claims. Applicant thus respectfully requests withdrawal of this rejection.

Rejections under 35 U.S.C. §103

Claims 17 and 18 have been rejected under 35 U.S.C. §103 as being obvious over Grabstein *et al.* (US Patent No. 5,162,111) further in view of Sampathkumar (US Patent No. 4,804,520). Applicant traverses this rejection.

As discussed above, Grabstein *et al.* do not teach or suggest methods for treating a localized bacterial infection, a bacterial-related disease, or both comprising locally administering a composition comprising a therapeutically effective amount of a GM-CSF polypeptide, or compositions comprising a therapeutically effective amount of a GM-CSF polypeptide for locally treating a localized bacterial infection, a bacterial related disease, or both, as recited by the currently pending claims. Sampathkumar fails to cure this deficiency.

The Examiner cites Sampathkumar for the teaching that diseases such as periodontal disease involve bacterial infection, that periodontal diseases affect the periodontum, which is the investing and supporting tissue surrounding a tooth, that gingivitis and periodontitis are inflammatory disorders of gingiva and the periodontal ligaments, respectively, and that oral cavity diseases which include gingivitis and periodontitis are initiated/and or perpetuated by bacteria in the oral cavity.

The disclosure of Sampathkumar is directed to pharmaceutical compositions comprising anaerobe-selective antibacterial agents which are substituted or unsubstituted 1,12-dodecanedioic peroxy acids, or their pharmaceutically-acceptable salts or esters (see Abstract). Nowhere does Sampathkumar teach or suggest methods comprising local administration of therapeutically effective amounts of GM-CSF, or compositions for local treatment comprising therapeutically effective amounts of GM-CSF, as recited by the currently pending claims. As such, Sampathkumar does not make up for the deficiency of Grabstein *et al.*

As such, neither Grabstein *et al.* nor Sampathkumar, either alone or in combination, renders obvious the currently pending claims. Applicant thus respectfully requests withdrawal of this rejection.

In light of the present amendments and arguments, Applicant submits that the present application is in condition for allowance, and respectfully requests a notice to that effect. If it would further prosecution or expedite allowance of the present case, the Examiner is invited to telephone the undersigned at 612-766-2071.

Please apply any charges, or credit any overpayments, to deposit account 06-1050, referencing Attorney Docket No. 15665-0010US1.

Respectfully submitted,

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